

What is claimed is:

1. A method for analyzing a sample containing biomolecules comprising the steps of
 - 5 providing a plurality of sample portions of a sample containing biomolecules;
 - acquiring one or more mass spectra of at least one of the sample portions;
 - analyzing the one or more mass spectra using at least one of an expression dependent based analysis, a mass spectrometric data based analysis, and a search
 - 10 results based analysis;
 - selecting one or more mass-to-charge ratio ranges based on the analysis of the one or more mass spectra;
 - acquiring a fragmentation spectrum of at least one of the sample portions at one or more of the selected one or more mass-to-charge ratio ranges;
 - 15 comparing the fragmentation spectrum of at least one of the selected one or more mass-to-charge ratio ranges to a database of known or predicted fragmentation mass spectra; and
 - determining whether a biomolecule is present in the sample based on the comparison.
- 20 2. The method of claim 1, wherein the biomolecules comprise at least one of proteins and peptides.
3. The method of claim 1, wherein the step of acquiring one or more mass spectra
25 comprises:
 - ionizing at least a portion of the biomolecules in a sample portion using matrix assisted laser desorption ionization; and
 - acquiring one or more mass spectra using a mass spectrometer.

4. The method of claim 3, wherein the mass spectrometer comprises a time-of-flight mass spectrometer.
- 5 5. The method of claim 1, wherein the step of analyzing the one or more mass spectra comprises determining an expression level ratio between one or more differentially labeled biomolecules in the sample portion.
6. The method of claim 5, wherein the step of selecting one or more mass-to-charge ratio ranges comprises selecting one or more mass-to-charge ratio ranges based on the expression level ratios of a mass signal in the one or more mass spectra.
- 10 7. The method of claim 5, further comprising a step of compensating for sample bias in one or more expression level ratios.
- 15 8. The method of claim 1, wherein the step of analyzing the one or more mass spectra comprises determining a signal intensity and a signal-to-noise ratio for the one or more mass signals in one or more mass spectra.
9. The method of claim 8, wherein the step of selecting one or more mass-to-charge ratio ranges comprises selecting one or more mass-to-charge ratio ranges based on the signal intensity and a signal-to-noise ratio for one or more mass signals in the one or more mass spectra.
- 20 10. The method of claim 1, wherein the step of analyzing the one or more mass spectra comprises comparing of at least a portion of one or more of the one or more mass spectra to one or more known or predicted mass spectra to assign one or more biomolecules as potential identifications of one or mass signals in the one or more mass spectra.
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11. The method of claim 10, wherein the step of selecting one or more mass-to-charge ratio ranges comprises selecting one or more mass-to-charge ratio ranges based on a confidence level associated with the one or more biomolecules assigned as potential identifications of one or mass signals in the one or more mass spectra.
12. The method of claim 10, wherein the step of analyzing the one or more mass spectra comprises comparing of at least a portion of one or more of the one or more mass spectra to one or more known or predicted mass spectra to assign one or more biomolecules as potential identifications of one or mass signals in the one or more mass spectra using a peptide mass fingerprinting technique.
13. The method of claim 1, wherein the step of acquiring a fragmentation spectrum comprises:
- ionizing at least a portion of the biomolecules in a sample portion using matrix assisted laser desorption ionization to produce sample ions;
 - separating sample ions using a first mass spectrometer;
 - fragmenting at least a portion of the sample ions in the selected one or more mass-to-charge ratio ranges; and
 - acquiring a fragmentation spectrum using a second mass spectrometer.
14. The method of claim 13, wherein the first mass spectrometer and second mass spectrometer comprises a tandem time-of-flight mass spectrometer system.
15. An article of manufacture comprising a computer-readable media with computer-readable instructions embodied thereon for performing the method of claim 1.
16. A method for analyzing a sample containing proteins comprising the steps of

- providing a plurality of sample portions each comprising a first sample containing at least one of peptides and proteins and a second sample containing at least one of peptides and proteins, at least a portion of the biomolecules in the first sample and the second sample being differentially labeled with an isotope coded reagent;
- 5 acquiring one or more mass spectra of at least one of the sample portions; determining an expression level ratio between one or more differentially labeled biomolecules in the sample portion;
- selecting one or more mass-to-charge ratio ranges based on the expression level ratios of a mass signal in the one or more mass spectra;
- 10 acquiring a fragmentation spectrum of at least one of the sample portions at one or more of the selected one or more mass-to-charge ratio ranges; comparing the fragmentation spectrum of at least one of the selected one or more mass-to-charge ratio ranges to a database of known or predicted fragmentation mass spectra; and
- 15 determining whether a biomolecule is present in the sample based on the comparison.
17. The method of claim 16, wherein the step of acquiring one or more mass spectra comprises:
- 20 ionizing at least a portion of the biomolecules in a sample portion using matrix assisted laser desorption ionization; and acquiring one or more mass spectra using a mass spectrometer.
- 25 18. The method of claim 17, wherein the mass spectrometer comprises a time-of-flight mass spectrometer.
19. The method of claim 16, further comprising a step of compensating for sample bias in one or more expression level ratios.

20. The method of claim 16, further comprising the step of determining a signal intensity and a signal-to-noise ratio for one or more mass signals in the one or more mass spectra
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21. The method of claim 20, wherein the step of selecting one or more mass-to-charge ratio ranges further comprises selecting one or more mass-to-charge ratio ranges based on the signal intensity and a signal-to-noise ratio for one or more mass signals in the mass spectrum.
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22. The method of claim 16, further comprising the step of comparing of at least a portion of one or more of the one or more mass spectra to one or more known or predicted mass spectra to assign one or more biomolecules as potential identifications of one or mass signals in the one or more mass spectra.
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23. The method of claim 22, wherein the step of selecting one or more mass-to-charge ratio ranges further comprises selecting one or more mass-to-charge ratio ranges based on a confidence level associated with the one or more biomolecules assigned as potential identifications of one or mass signals in the one or more mass spectra.
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24. The method of claim 22, wherein the step of analyzing the one or more mass spectra comprises comparing of at least a portion of one or more of the one or more mass spectra to one or more known or predicted mass spectra to assign one or more biomolecules as potential identifications of one or mass signals in the one or more mass spectra using a peptide mass fingerprinting technique.
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25. The method of claim 16, wherein the step of acquiring a fragmentation spectrum comprises:

- ionizing at least a portion of the biomolecules in a sample portion using matrix assisted laser desorption ionization to produce sample ions;
separating sample ions using a first mass spectrometer;
fragmenting at least a portion of the sample ions in the selected one or
5 more mass-to-charge ratio ranges; and
acquiring a fragmentation spectrum using a second mass spectrometer.
26. The method of claim 25, wherein the first mass spectrometer and second mass spectrometer comprises a tandem time-of-flight mass spectrometer system.
- 10 27. An article of manufacture comprising a computer-readable media with computer-readable instructions embodied thereon for performing the method of claim 16.
28. A method for analyzing a sample for at least one biomolecule comprising the
15 steps of
depositing at least one sample portion on a solid support;
vaporizing at least a portion of the sample portion by matrix
assisted laser desorption ionization to form a first vaporized ionized
sample;
20 processing at least a portion of the first vaporized ionized sample with a mass spectrometry apparatus to determine a first data set comprising a list of ion abundances as a function of ion mass-to-charge ratio of the first vaporized ionized sample;
comparing the first data set with at least one of a second data set which
25 identifies biomolecules by ion abundance as a function of ion mass-to-charge ratio;
selecting one or more ion mass-to-charge ratio ranges for further analysis based on the comparison;
vaporizing at least another portion of the biological sample by matrix

assisted laser desorption ionization to form a second vaporized ionized sample;
processing at least a portion of the second vaporized ionized sample with
a mass spectrometry apparatus adjusted based on the first data set thereby to
determine a third data set comprising a list of ion abundance as a function of ion
5 mass-to-charge ratio of the second vaporized ionized sample; and performing at
least one of the steps of:

comparing the third data set with a fourth data set which identifies
biomolecules by ion abundance as a function of ion mass-to-charge ratio,
and using the identified biomolecules data and the first data set to obtain
10 quantitative information on the one or more biomolecules in the sample.

29. The method of any one of claims 28, wherein at least one first vaporized
biomolecule having a low concentration in the sample is processed as a second
vaporized ionized sample prior to processing a biomolecule having a higher
15 concentration in the sample than the first vaporized biomolecule.

30. An article of manufacture comprising a computer-readable media with computer-
readable instructions embodied thereon for performing the method of claim 28.